# SESSION VI

## HEART
## CARDIOVASCULAR AND RESPIRATORY REGULATION

Thursday (September 16, 2021; 9:45 – 17:30)

Chair:

Prof. Barbara Malinowska
Department of Physiology and Experimental Pathophysiology,
Medical University of Bialystok, Bialystok, Poland

Prof. Agnieszka Cudnoch-Jedrzejewska
Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Sciences, Medical University of Warsaw, Warsaw, Poland

Prof. Katarzyna Kaczynska
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# DETAILED SESSION VI SCHEDULE

## Part I – **HEART. CARDIOVASCULAR REGULATION.**

**Opening lectures** (Thursday, September 16, 2021; 11:30 – 13:00; *virtual stream A*)

S6.L1 IS OXYGEN STARVATION RESPONSIBLE FOR PROGRESSION TO RIGHT VENTRICULAR FAILURE IN PULMONARY ARTERIAL HYPERTENSION? **M. Okninska, Z. Zambrowska, A. Paterek, U. Mackiewicz, M. Maczewski** (Department of Clinical Physiology, Centre of Postgraduate Medical Education, Warsaw, Poland).

S6.L2 PURINERGIC SIGNALING AND ITS DISTURBANCES IN THE PATHOLOGY OF VESSELS AND HEART VALVES. **R.T. Smolenski** (Department of Biochemistry, Medical University of Gdansk, Gdansk, Poland)

S6.L3 HIGH SALT INTAKE PROMOTES ENDOTHELIAL DYSFUNCTION AND IMPAIRS BRAIN FUNCTION. ROLE OF THE IMMUNE SYSTEM. **A. Sawicka, M. Aleksandrowicz, E. Kozniewska** (Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland)

S6.L4 RECIPROCAL RELATIONSHIP BETWEEN ARTERIAL BLOOD PRESSURE AND GUT MICROBIOTA. **M. Ufnal, K. Jaworska, D. Chabowski** (Department of Experimental Physiology and Pathophysiology, Medical University of Warsaw, Warsaw, Poland)

**Oral presentations** (Thursday, September 16, 2021; 13:00 – 14:50; *virtual stream A*)

S6.L5 ROLE OF STEAROYL-COA DESATURASE 1 IN CONTROL OF THE HEART FUNCTION THROUGH LIPID METABOLISM CHANGES IN HYPERTHYROIDISM. **A. Olichwier[1], A. Binczak[2], M. Duda[2], P. Dobrzyn[1]** ([1]Nencki Institute of Experimental Biology, Warsaw, Poland, [2]Medical Center of Postgraduate Education, Warsaw, Poland).

S6.L6 STEAROYL-COA-DESATURASE 1 AFFECTS DAMAGED MITOCHONDRIAL DYNAMICS AFTER DOXORUBICIN TREATMENT. **O. Blesznowska, V. Baltskyi, A. Olichwier, P. Dobrzyn** (Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland).

S6.L7 THE EFFECT OF ISOPROTERENOL ON THE DEVELOPMENT OF HEART FAILURE IN C57BI/6J MICE. **A. Jedrzejewska, M. Zabielska-Kaczorowska, P. Mierzejewska, B. Kutryb-Zajac, O. Krol, E. M. Slominska, R.T. Smolenski** ([1]Department of Biochemistry, Medical University of Gdansk, Poland, [2]Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S6.L8 THE EFFECT OF KISSPEPTIN-10 ON THE REGULATION OF COLLAGEN METABOLISM IN THE HEART. **P. Radwanska, M. Galdyszynska, L. Piera, J. Drobnik** (Department of Pathophysiology, Chair of General and Experimental Pathology, Medical University of Lodz, Lodz, Poland).

S6.L9 THE INFLUENCE OF GUT DYSBIOSIS CAUSED BY HIGH FAT DIET ON THE MYOCARDIAL FUNCTION. **P. Dubinski[1], K. Czarzasta[1], D. Sztechman[1], L. Puhalska[1], D. Mirowska-Guzel[2], A. Cudnoch-Jedrzejewska[1]** ([1]Chair and Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland, [2]Department of Experimental and Clinical Pharmacology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland).

S6.L10 EFFECTS OF PERIPHERAL $CB_1$ RECEPTOR INVERSE AGONIST JD5037 IN MONO- AND POLYTHERAPY WITH METFORMIN IN A MONOCROTALINE-INDUCED RAT MODEL OF PULMONARY ARTERIAL HYPERTENSION. **P. Remiszewski, A. Pedzinska-Betiuk, K. Minczuk, J. Weresa, A. Krzyzewska, B. Malinowska** (Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.L11 HOW BEETROOT JUICE NITRATES CAN MODULATE THE FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM? A THEORETICAL FRAMEWORK. **M. Wyciszkiewicz, R. Seredynski, B. Paleczny, B. Ponikowska** (Wroclaw Medical University, Wroclaw, Poland).

*Questions and answers. Session summary.*

## Part II – **CARDIO-RESPIRATORY REGULATION**

**Opening lecture** (Thursday, September 16, 2021; 14:55 – 15:25; *virtual stream A*):

S6.L12 BREATHING DISORDERS IN ALZHEIMER'S DISEASE. **K. Kaczynska, K. Andrzejewski** (Mossakowski Medical Research Institute Polish Academy of Sciences, Warsaw, Poland).

**Oral presentations** (Thursday, September 16, 2021; 15:25 – 16:15; *virtual stream A*):

S6.L13 DEFICIT OF MONOAMINES IN RESERPINE PARKINSON'S DISEASE MODEL ALTERS THE HYPOGLOSSAL NERVE ACTIVITY. **K. Andrzejewski[1], M. Jampolska[1], M. Zaremba[2,3], I. Joniec-Maciejak[2], M. Orlowska[1], K. Kaczynska[1]** ([1]Department of Respiration Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [2]Department of Experimental and Clinical Pharmacology, Centre for Preclinical Research (CePT), Medical University of Warsaw, Warsaw, Poland, [3]Laboratory of Experimental Therapies, Military Institute of Hygiene and Epidemiology, Warsaw, Poland).

S6.L14 DAILY SITTING TIME AFFECTS LACTULOSE-INDUCED CHANGES IN HYPOXIC RESPONSIVENESS IN HUMANS. **K. Pawlowska-Seredynska[1], R. Seredynski[2], B. Ponikowska[2], W. Umlawska[1], B. Paleczny[2]** ([1]Department of Human Biology, University of Wroclaw, Wroclaw, Poland; [2]Department of Physiology, Wroclaw Medical University, Wroclaw, Poland).

S6.L15 VASOPRESSIN AND V1a RECEPTORS IN HEMODYNAMIC AND RESPIRATORY REGULATION IN NORMOTENSIVE AND HYPERTENSIVE RATS. **M. Proczka[1], A. Trzcinski[2], T. Zera[2]** ([1]Department of Experimental and Clinical Physiology, Doctoral School, Medical University of Warsaw, Poland, [2]Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Poland).

*Session summary*

**Poster session** – Part I (Thursday, September 16, 2021; 9:45 – 11:20; *virtual stream C*)

S6.P1 CHEMOSENSITIVITY DURING MECHANO AND METABOREFLEX ACTIVATION IN HEALTHY SUBJECTS CHARACTERIZED BY LOW AND HIGH EXERCISE CAPACITY. **W. Lopusiewicz, A. Lis, T. Okupnik, B. Paleczny, B. Ponikowska** (Wroclaw Medical University, Poland)

S6.P2 CARDIAC PHYSIOLOGY AFTER OSTARINE TREATMENT – *IN VITRO* STUDY ON H9C2 CARDIOMYOCYTES AND FIBROBLASTS. **N. Leciejewska[1], P. A. Kolodziejski[1], E. Malek[2], K. Mielnik[1], E. Pruszynska-Oszmalek[1]** ([1]Department of Animal Physiology, Biochemistry and Biostructure, Poznan University of Life Sciences, Poznan, Poland, [2]Department of Preclinical Sciences and Infectious Diseases, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland).

S6.P3 EVALUATION OF THE ANTI-INFLAMMATORY AND ANTI-PROLIFERATIVE PROPERTIES OF CANNABIDIOL IN AN EXPERIMENTAL MODEL OF MONOCROTALIN-INDUCED PULMONARY HYPERTENSION. **A. Krzyzewska[1], M. Baranowska-Kuczko[1,2], I. Kasacka[3], H. Kozlowska[1]** ([1]Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland, [2]Department of Clinical Pharmacy, Medical University of Bialystok, Bialystok, Poland, [3]Department of Histology and Cytophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.P4 THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS ANACETRAPIB AND TORCETRAPIB ON LIVER DDAH1 ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA. **E. Krzewicka-Romaniuk, D. Siedlecka, A. Pradiuch, G. Wojcicka** (Department of Pathophysiology, Medical University of Lublin, Lublin, Poland).

S6.P5 THE CHARACTERISTICS OF A SUB-CHRONIC MODEL OF NON-ATOPIC ASTHMA. **D. Zajac, E. Russjan, K. Kaczynska** (Department of Respiration Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S6.P6 THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS, ANACETRAPIB AND TORCETRAPIB, ON PLASMA AND LIVER PARAOXONASE 1 (PON 1) ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA. **D. Siedlecka, E. Krzewicka-Romaniuk, A. Pradiuch, G. Wojcicka** (Department of Pathophysiology, Medical University of Lublin, Lublin, Poland).

S6.P7 LONG-TERM EFFECT OF PERIPARTUM DEPRESSION ON THE CARDIOVASCULAR SYSTEM OBSERVED IN THE ADULT RAT FEMALE OFFSPRING. **J. Kruszewska[1], D. Sztechman[1], V. Skital[1], J. Malik[1], A. Segiet-Swiecicka[1], K. Czarzasta[1], E. Sajdel-Sulkowska[2]** ([1]Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland; [2]Department of Psychiatry, Harvard Medical School, Boston, MA, USA).

S6.P8 ELECTROPHYSIOLOGICAL, HEART RATE VARIABILITY, AND BIOCHEMICAL DISTURBANCES IN A RAT MODEL OF 5-FLUOROURACIL INDUCED CARDIOTOXICITY ARE PARTIALLY REVERSED BY CHRONIC VITAMIN D SUPPLEMENTATION. **M. Jurczyk[1], P. Stach[1], V. Aleksandrovych[1], A. Midro[1], M. Krol[1], B. Kusnierz-Cabala[2], P. Mazur[3], K. Jasinski[4], A. Poniatowski[1], K. Gil[1]** ([1]Department of Pathophysiology, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Diagnostics, Chair of Clinical Biochemistry, Jagiellonian University Medical College, Krakow, Poland, [3]Department of Medical Diagnostics, Faculty of Pharmacy, Jagiellonian University Medical College, Krakow, Poland, [4]Institute of Nuclear Physics of the Polish Academy of Sciences, Department of Magnetic Resonance Imaging, Krakow, Poland).

S6.P9 TUMOUR NECROSIS FACTOR RECEPTORS TYPE 1 AND TYPE 2 ARE EXPRESSED IN THE BRAINSTEMS OF NORMOTENSIVE AND HYPERTENSIVE RATS. **A. Segiet-Swiecicka[1], K. Czarzasta[1], T. Zera[1]** ([1]Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland).

S6.P10 DEVELOPMENT OF HEART FAILURE IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). **O. Krol[1], P. Mierzejewska[1], M. Zabielska-Kaczorowska[1,2], T. Borkowski[3], A. Jedrzejewska[1], E. M. Slominska[1], R.T. Smolenski[1]** ([1]Department of Biochemistry, Medical University of Gdansk, Gdansk, Poland, [2] Department of Physiology, Medical University of Gdansk, Gdansk, Poland, [3]Department of Medical Laboratory Diagnostics, Medical University of Gdansk, Gdansk, Poland).

S6.P11 STEAROYL-COA DESATURASE 4 DEFICIENCY PROTECTS AGAINST HIGH FAT DIET-INDUCED HEART DYSFUNCTION IN MOUSE. **M. Wolosiewicz[1], A. Filip[1], M. Duda[2], A. Olichwier[1], V. Navrulin[1], P. Dobrzyn[1]** ([1]Laboratory of Molecular Medical Biochemistry, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [2]Department of Clinical Physiology, Postgraduate Medical School, Warsaw, Poland).

S6.P12 ASSOCIATION BETWEEN DEPRESSION AND UNFAVORABLE NUTRITIONAL, CARDIAC AND LABORATORY OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE. **G. Opielak[1], T. Powrozek[1], A. Skwarek-Dziekanowska[2], G. Sobieszek[2], T. Malecka-Massalska[2]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Department of Cardiology, 1st Military Clinical Hospital with the Outpatient Clinic, Lublin, Poland).

S6.P13 RELATION BETWEEN THE HEART RHYTHM ASYMMETRY AND THE RESPIRATORY PHASE IN HEALTHY PEOPLE AND PATIENTS WITH ARTERIAL HYPERTENSION. **D. Wejer[1], B. Graff[2], G. Graff[3], K. Narkiewicz[2], D. Makowiec[4]** ([1]University of Gdansk, Faculty of Mathematics, Physics and Informatics, Institute of Experimental Physics, Gdansk, Poland, [2]Medical University of Gdansk, Department of Hypertension and Diabetology, Gdansk, Poland, [3]Gdansk University of Technology, Faculty of Applied Physics and Mathematics, Gdansk, Poland, [4]University of Gdansk, Faculty of Mathematics, Physics and Informatics, Institute of Theoretical Physics and Astrophysics, Gdansk, Poland).

**Poster session** – Part II (Thursday, September 16, 2021; 16:30 – 17:30; *virtual stream C*)

S6.P14 POST-EXERCISE HYPOTENSION IN ELDERLY: THE EFFECT OF SINGLE SESSION OF WATER BASED EXERCISE. **C. Reis[1], W. Barbosa[1], L. Barcellos[1], P. Zovico[1], C. Leite[1], R. Rica[2], D. Bocalini[1]** ([1]Federal University of Espirito Santo, Vitoria, Brazil, [2]Estacio de Sa University, Vitoria, Brazil).

S6.P15 THE EFFECTS OF ENHANCED ENDOCANNABINOID TONE INDUCED BY CHRONIC ADMINISTRATION OF DUAL FAAH/MAGL INHIBITOR JZL195 IN SPONTANOUSLY HYPERTENSIVE RATS. **M. Toczek, A. Kicman, B. Malinowska** (Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.P16 EFFECT OF MUSIC ON TRAINING PARAMETERS AND MOOD STATE IN HIIT BODY WORK SESSIONS. **P.V.C. Zovico[1], R.A.A. Filho[1], J.J.G. Oliveira[1], W.A Barbosa[1], R.L. Rica[2], D.S. Bocalini[1]** ([1]Federal University of Espirito Santo, Vitoria, Brazil, [2]Estacio de Sa University, Vitoria, Brazil).

S6.P17 THE EFFECT OF GENETICALLY ALTERED AMP DEAMINASE ACTIVITY IN EXPERIMENTAL ISOPROTERENOL-INDUCED HEART FAILURE. **M. Zabielska-Kaczorowska[1,2], P. Mierzejewska[1], E.M. Slominska[1], R.T. Smolenski[1]** ([1]Department of Biochemistry, Medical University of Gdansk, Gdansk, Poland, [2]Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S6.P18 THE INFLUENCE OF CANNABIDIOL ON ISOLATED RAT ATRIA UNDER NORMOXIC, HYPOXIC AND REOXYGENATION CONDITIONS. **A. Pedzinska-Betiuk, J. Weresa, B. Malinowska** (Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.P19 NEUROPEPTIDE FF COUNTERACTS OPIOID INDUCED RESPIRATORY DEPRESSION. **P. Wojciechowski, K. Andrzejewski, K. Kaczynska** (Department of Respiration Physiology, Mossakowski Medical Research, Institute Polish Academy of Sciences, Warsaw, Poland).

S6.P20 INFLUENCE OF CANNABINOID CB1 AND CB2 RECEPTOR ANTAGONISTS ON CARDIOSTIMULATORY EFFECTS OF ISOPRENALINE IN HUMAN ATRIAL TRABECULAE. **J. Weresa, A. Pedzinska-Betiuk, B. Malinowska** Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.L1

# IS OXYGEN STARVATION RESPONSIBLE FOR PROGRESSION TO RIGHT VENTRICULAR FAILURE IN PULMONARY ARTERIAL HYPERTENSION?

M. OKNINSKA, Z. ZAMBROWSKA, A. PATEREK, U. MACKIEWICZ, M MACZEWSKI

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Pulmonary arterial hypertension (PAH) initially results in compensatory right ventricular (RV) hypertrophy, but eventually in RV failure. This transition is poorly understood, but may be triggered by hypoxia. Indeed in PAH oxygen delivery is impaired due to increased extravascular compression of RV coronary vessels (due to both RV hypertrophy and increased RV pressures) and reduced coronary perfusion pressure (due to reduced aortic pressure as a consequence of reduced LV cardiac output), while increased RV afterload results in proportionally increased energy demand. Last but not least, capillary rarefaction was found in various animal PAH models as well as in humans. We have recently demonstrated that in PAH RV $pO_2$ is reduced by almost half, while that in LV is maintained. Acute administration of new agent that facilitates oxygen dissociation from hemoglobin, myo-inositol trispyrophosphate (ITPP), partially restored RV $pO_2$, providing beneficial effects on RV contractility. This indicates that oxygen balance is impaired in PAH and as such can be an important target for PAH therapy. ITPP may be one of such potential therapies.

S6.L2

# PURINERGIC SIGNALLING AND ITS DISTURBANCES IN THE PATHOLOGY OF VESSELS AND HEART VALVES

R.T. SMOLENSKI

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Purinergic signaling is primarily attributed to function of purinergic receptors that respond to nucleotide ligands such as adenosine triphosphate (ATP) P2 receptors or nucleosides such as adenosine P1 receptors. However, purinergic signaling is far more complex. First, many other compounds are involved as signaling molecules that include pyrimidine nucleotides such as UTP or nicotinamide derivatives. Then, origin of purinergic mediators could involve intracellular pathways with its release into extracellular space or formation of purinergic mediators in the extracellular space. This underlies the importance of membrane transport systems such as nucleoside transporters for adenosine or pannexin channels for ATP. Purinergic signaling is tightly controlled by ectoenzymes such as ecto-nucleoside triphosphate diphosphohydrolases (eNTPD) and ecto-5'-nucleotidase (e5'NT). Our group identified also another element of the ectoenzyme cascade that is involved in modulation of purinergic system which is ecto-adenosine deaminase (eADA). Purinergic signaling controls broadest range of physiological functions of the organisms and different elements often induce opposite effects. For instance activation of P2 receptors stimulates platelet aggregation while activation of P1 receptors has anti-platelet effect. This provides broad range of therapeutic opportunities, but this is also important disadvantage as it is difficult to achieve specificity and avoid unwanted effects. Despite that, there are several success stories of clinical applications with anti-platelet drug clopidogrel (P2Y12 receptor antagonist) as an as an example. Purinergic signaling is especially important in vascular pathologies. Our group identified purinergic receptors and ectoenzymes on the surface of cellular elements of the aortic valves. Activity of e5'NT responsible for adenosine production on the surface of the aortic leaflets was found to be the highest in the human body. We found profound alterations of the ectoenzymes activities on the surface of the aortic valves in calcific aortic valve disease in humans which include reduction of e5'NT activity and elevation of eADA activity. Mice genetically altered to delete e5'NT activity was found to develop alterations of aortic valve leaflets. This has several practical implications: genetic variations of purinergic receptors or enzymes could relate to valve disease. Purinergic drugs (clopidogrel, ticagrelor, ticlopidine, dipyridamole, deoxycoformycin or newer A1 or A2b activators) could be effective in prevention of aortic valve disease. Finally, prevention of degeneration of implanted biological valves could be achieved by its engineering to enhance adenosine production and to block ATP/ADP signaling.

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S6.L3

# HIGH SALT INTAKE PROMOTES ENDOTHELIAL DYSFUNCTION AND IMPAIRS BRAIN FUNCTION. ROLE OF THE IMMUNE SYSTEM

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consumption of sodium chloride (HSD) is well known risk factor for cardiovascular diseases including hypertension and ischemic stroke. We, and others have documented that long lasting HSD leads to dysfunction of the endothelium manifested by a decreased shear stress-dependent production of a potent vasodilator nitric oxide (NO) and decreased response of brain blood vessels to endothelium-dependent vasodilators in rodents, in the absence of increased blood pressure. One of the reasons why HSD leads to endothelial dysfunction may be damage of the endothelial glycocalyx which plays essential role in shear stress activation of endothelial NO synthase. Dysfunction of the endothelium may lead to the impairment of functional hyperemia and produce symptomatic neuronal dysfunction. Recently, neuronal dysfunction and cognitive impairment was reported in rats fed HSD for several weeks. It is not known, however, how excess dietary salt leads to NO deficit and vascular morphological changes as there is no increase in plasma concentration of sodium ions during consumption of HSD. This challenges the direct effect of sodium ions on blood vessels. Considering that gastrointestinal tract is in direct contact with ingested sodium, the participation of the gut microbiota cannot be excluded. Particularly, in view of the results reported in the literature demonstrating that HSD may lead to the increase of plasma trimethylamine N-oxide (TMAO) concentration and gut dysbiosis. We were, however, unable to demonstrate an increase in TMAO plasma concentration in the rats fed HSD for 4 weeks. Recently published results convincingly demonstrate that dietary salt promotes neurovascular and cognitive impairment through a gut initiated TH17 response.

*Acknowledgements*: The research was supported by the KNOW-MMRC project.

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S6.L4

# RECIPROCAL RELATIONSHIP BETWEEN ARTERIAL BLOOD PRESSURE AND GUT MICROBIOTA

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Trillions of microbes inhabit the human gut. Recent scientific advances demonstrate that their role goes beyond assisting in food breakdown and nutrient extraction. Metabolites produced by commensal microbiota are beginning to be recognized as biologically active compounds. Given the striking similarity of the gut microbiota-derived metabolites to the signaling molecules generated natively by the host, the microbiota can orchestrate a plethora of responses from the host and recognize and respond to endogenous signals. For instance, short-chain fatty acids, which are the products of dietary fiber bacterial fermentation, have been found to dilate blood vessels and lower blood pressure, whereas trimethylamine, a gut bacteria metabolite of carnitine and choline, has recently emerged as a potentially toxic molecule. The interaction between the host and gut bacteria is bidirectional. On the one hand, gut bacteria may affect the host's homeostasis *via* blood-borne bacterial products. On the other, the host can affect the gut bacteria by dietary habits and ingestion of antibacterial food preservatives, medicinal products, or other substances that may alter the gut environment. To enter the bloodstream, microbiota products cross the gut-blood barrier, a multilayer system of the intestinal wall. Experimental and clinical studies show that cardiovascular diseases may compromise the gut-blood barrier function and increase gut-to-blood penetration of microbiota-derived molecules. This paper explores how gut microbiota-derived metabolites impact the regulation of arterial blood pressure. It also discusses recent findings demonstrating how hypertension-induced changes in intestines may affect gut microbiota composition.

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S6.L5

# ROLE OF STEAROYL-COA DESATURASE 1 IN CONTROL OF THE HEART FUNCTION THROUGH LIPID METABOLISM CHANGES IN HYPERTHYROIDISM

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[1]Nencki Institute of Experimental Biology, Warsaw, Poland, [2]Medical Center of Postgraduate Education, Warsaw, Poland

Thyroid hormones (TH) and stearoyl-CoA desaturase 1 (SCD1), an enzyme responsible for monounsaturated fatty acids (FAs) synthesis, are both involved in reprograming of cardiac metabolism, what affects heart function and structure. TH *via* thyroid hormone receptors (TR) can modulate expression of the genes involved in heart function, e.g. myosin heavy chain α and β (*Myh6* and *Myh7*) and lipid metabolism, e.g. fatty acid synthase (*Fas*) and sterol regulatory element-binding protein 1 (*Srebf*). The mechanism identifying the role of TH-SCD1 cross-talk in the control of heart work is still unknown. Therefore, the aim of the presented study was to determine the interrelation between SCD1 and TH in the regulation of the lipid metabolism and heart function in hyperthyroidism. To induce hyperthyroidism wild type (WT) and SCD1$^{-/-}$ mice were injected with triiodothyronine (T3). Performed analyses show increase of T3 and free T3 plasma level both in WT and SCD1$^{-/-}$ hyperthyroid mice and additional elevation of thyroid stimulating hormone (TSH) in SCD1$^{-/-}$ mice. Ablation of SCD1 in hyperthyroidism led to decrease in the left ventricle (LV) end-diastolic dimension with a simultaneous increase in LV wall thickness and an improvement in systolic and diastolic functions, when compared to WT littermates. Moreover, decreased triglyceride content was observed in hyperthyroid SCD1$^{-/-}$ mice, unlike to increase of FAs and diacylglycerol in hyperthyroid WT. Those changes were caused by simultaneous activation of lipolysis (increase of adipose tissue specific triglyceride lipase (ATGL) and elevated phosphorylation of hormone-sensitive lipase (HSL)) and lipogenesis (elevated SREBP-1 and FAS protein levels) in WT hyperthyroid mice, in contrast to activated only lipolysis in SCD1$^{-/-}$ hyperthyroid mice. Furthermore, changes in lipid metabolism were associated with increase in TRα and TRβ protein levels in WT hearts after TH administration, what was not observed in SCD1$^{-/-}$ mice. Additionally, in hyperthyroid SCD1$^{-/-}$ hearts, *Myh6* expression was not changed, what is consistent with unchanged TR levels. Collectively, these results indicate that SCD1 is a key factor in the regulation of TH-dependent changes in lipid metabolism in cardiomyocytes, what can affect heart function, structure and contractility.

*Acknowledgements*: National Science Center (Poland) grants UMO-2014/13/B/NZ4/00199 and UMO-2017/27/N/NZ4/01995.

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S6.L6

# STEAROYL-COA-DESATURASE 1 AFFECTS DAMAGED MITOCHONDRIAL DYNAMICS AFTER DOX TREATMENT

O. BLESZNOWSKA, V. BALTSKYI, A. OLICHWIER, P. DOBRZYN

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Doxorubicin (DOX) is a widely used drug in cancer therapy which also exerts cardiotoxic effects. DOX affects function and structure of mitochondria in cardiomyocytes and thus causes changes in mitochondrial dynamics, ATP production and oxidative phosphorylation chain (OXPHOS). One of the main lipogenic enzyme, stearoyl-CoA-desaturase 1 (SCD1) is an important point in regulation of heart function and structure, however its role in DOX induced cardiotoxicity is unknown. Therefore, the aim of the present study was to determine if SCD1 is involved in regulation of mitochondrial structure, dynamics and activity, and development of cardiomyocytes dysfunction caused by DOX. Murine HL-1 cardiomyocytes were treated with DOX and SCD1 inhibitor A939572. Performed analyses show that SCD1 inhibition in cardiomyocytes increases number of mitochondria, modulates their shape and does not affect mitochondrial membrane potential. Interestingly, SCD1 inhibition in DOX treated cardiomyocytes increases number of mitochondria when compared to DOX condition. Additionally SCD1 inhibition decreases expression of mitochondrial fission genes Mfn1 and Mfn2 reversing upregulation caused by DOX. Mitochondrial homeostasis disruption is associated with changes in mitochondrial structure and activity, ATP production and anion transporting protein levels (e.g. uncoupling protein 3 (UCP3)). Blocked SCD1 activity in DOX condition elevates UCP3 protein level and reduces ATP production. Moreover DOX treatment decreases protein level of complex 1 (OXPHOS chain) and SCD1 inhibition reverses this effect. ATP production is related to peroxisome proliferator-activated receptor alpha (PPARα), transcription factor that is involved in control of β-oxidation of fatty acids (FAs) in mitochondria. Elevated PPARα protein level and decreased free FAs level was observed in cardiomyocytes treated with both DOX and SCD1 inhibitor when compared to cardiomyocytes treated only with DOX. Obtained results suggest that SCD1 inhibition can improve and stabilize mitochondrial functionality after DOX treatment.

*Acknowledgements*: National Science Center (Poland) grant UMO-2016/22/E/NZ4/00650.

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S6.L7

# THE EFFECT OF ISOPROTERENOL ON THE DEVELOPMENT OF HEART FAILURE IN C57BI/6J MICE

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Isoproterenol is a nonselective beta-adrenergic agonist used widely for inducing heart failure in mice. The main purpose of this study was to confirm the cardiotoxicity of isoproterenol based on in vitro and in vivo models. *In-vitro* model: to analyze the mitochondrial function rat cardiomyocytes (H9c2 cells) were cultured in a DMEM medium. The mitochondrial function was assessed using the Agilent Seahorse XF Cell Mito Stress equipment after 48 h treatment with 10, 20, 50 and 100 μM isoproterenol. Respiration was quantified by sequential addition of 1.5 μM oligomycin, 1.0 μM FCCP, and 0.5 μM rotenone with antimycin B. *In-vivo* model: male mice (n=4–6) were treated with isoproterenol (100 mg/kg) administered subcutaneously for 4 or 8 days. For the transthoracic echocardiography, mice were anesthetized with ketamine (100 mg/kg) and xylazine (10 mg/kg) intraperitoneally. After chest hair removal, animals were placed on a heated platform to maintain the body temperature at 37°C. The transducer was placed above the anterior chest wall and hemodynamic parameters, including stroke volume (SV), left ventricular ejection fraction (EF) and fractional shortening (FS) as well as cardiac output (CO) and left ventricular (LV) Mass were collected. The statistical analysis was performed using Graph Pad Prism 7 (Graph Pad Software). Paired Student t-test was used for comparisons between two groups. A p-value $<0.05$ was considered a significant difference. The analysis of the mitochondrial function of the H9c2 cells showed a significant reduction in the oxygen consumption rate (OCR) at 50 μM isoproterenol treatment. This dose caused a significant reduction in basal respiration ($p<0.01$), as well as ATP-linked respiration ($p < 0.001$). Interestingly, the 100 μM dose turned out to be toxic to the H9c2 cells. After 4 days of treatment, no deterioration in cardiac function was observed. Furthermore, a significant decrease in EF ($p<0.001$) and FS ($p<0.05$), and an increase of LV Mass ($p<0.05$) was observed after 8 days compared to the control group. These results indicate the deterioration of left ventricular function induced by the 8-day administration of isoproterenol. Based on *in vitro* and *in vivo* studies, we have shown that isoproterenol reduces heart function and develops heart dysfunction both at the structural and cellular levels.

*Acknowledgements*: Preludium 2018/29/N/NZ4/02259, HARMONIA 2016/22/M/NZ4/00678.

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S6.L8

# EFFECT OF KISSPEPTIN-10 ON THE REGULATION OF COLLAGEN METABOLISM IN THE HEART

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Myocardial fibrosis is connected with remodeling of the connective tissue of the heart. It is mainly caused by overproduction of collagen by fibroblasts. The main factors that regulate collagen metabolism in the heart include cytokines, endopeptidases, reactive oxygen species and hormones. Kisspeptin-10 (KiSS-10) is the product of the *kiss-1* gene and belongs to the RF-amide peptide family. The aim of the present study was determination of the collagen metabolism in cardiac fibroblasts under the influence of KiSS-10. The effect of KiSS-10 on collagen metabolism within the heart of mice was also examined. The experiments were performed on human cardiac fibroblast cell line and male BALB/c mice. This *in vitro* model was used to assess intracellular collagen content, expression of α1 chains of procollagen type I and III, C-terminal propeptides of procollagen type I and III (PICP and PIIICP), metalloproteinases (MMP-1, -2, -9), tissue inhibitors of metalloproteinases (TIMPs 1-4), transforming growth factor β1 (TGF-β1). The *in vivo* studies were carried out to determine the serum level of PICP and PIIICP. The collagen content and expression of α1 chains of procollagen type I and III within the hearts of mice were also measured. KiSS-10 significantly elevates the content of collagen in the heart and cardiac fibroblasts cultures. These changes correlate with an increase in the level of the PICP and PIIICP in human cardiac fibroblast culture medium as well as mouse PIIICP in serum. *In vitro*, this hormone inhibits the release of matrix metalloproteinases (MMP-1, -2, -9) and stimulates the secretion of their tissue inhibitors (TIMP-1, -2, -4). KiSS-10 also increases the expression of α1 chains of procollagen type I and III *in vitro*. However, the introduction of KiSS-10 to the cardiac fibroblasts cultures does not affect release of TGF-β1. The results indicate that KiSS-10 is involved in the regulation of heart fibrosis. Augmentation, by KiSS-10, of the collagen deposition is dependent on the protein synthesis elevation, inhibition of matrix metalloproteinases (increase of TIMPs release) or decrease of matrix metalloproteinases (MMP-1, 2, 9) concentration. The effect of KiSS-10 is related to direct action of this compound on cardiac fibroblasts. However, the profibrotic activity of KiSS-10 is not dependent on release of TGF-β1. The present study points at KiSS-10 as the novel target for antifibrotic therapy.

This research was supported by the National Science Centre, Poland (grant no. 2018/02/X/NZ5/03158).

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S6.L9

# INFLUENCE OF GUT DYSBIOSIS CAUSED BY HIGH FAT DIET ON THE MYOCARDIAL FUNCTION

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High fat diet can induce intestinal dysbiosis and lead to chronic, systemic inflammation that affects myocardial function. The aim of the project was to investigate whether the pro-inflammatory effects of intestinal dysbiosis and a high fat diet are related to dysfunction of the rat heart muscle. The studies were conducted on 15 male Sprague Dawley rats, divided into the two groups: rats on normal fat diet (NFD), n=7, contained: 3.6% fat, 17.4% protein, 60% carbohydrates, 0.2% sodium, 2864 kcal/kg (Labofeed B, Kcynia, Poland), and rats on high fat diet (HFD), n=7, contained: 31% fat, 17.1% protein, 35.5% carbohydrates, 0.18% sodium, 3842kcal/kg (Laboffed B, Kcynia, Poland). Faeces for microbiota analysis were collected from randomly selected 12-week old rats on NFD (n=3) and on HFD (n=3). The same rats on NFD (n=3) and HFD (n=3) from which feces were collected for microbiological analysis were subjected to the ECHO study. Immediately after ECHO test all rats on NFD (n=7) and on HFD (n=7) were euthanized in order to plasma and left ventricular (LV) tissue collection for biochemical analysis. The multiplex real time PCR analysis was conducted for determining the rat TLR4 and TLR6 receptor. Plasma LPS concentrations were also determined using ELISA. In the fecal cultures of NFD rats, there were obtained a higher number of bacteria in the phylum *Proteobacteria*: *Escherichia coli* and phylum *Firmicutes*: *Enterococcus spp*. Whereas in the fecal cultures of HFD rats were received a higher number of bacteria in the phylum *Bacteroidetes*: *Bacteroides spp*. In the ECHO analysis in the HFD rats were noted mild generalized LV hypertrophy accompanied by a larger left atrium. Additionally, left ventricular diastolic dysfunction was also indicated in the HFD rats in comparison with the NFD rats. RT-PCR analysis showed significantly higher expressions of TLR4 mRNA and TLR6 mRNA in the LV in the HFD rats compared to the NFD rats. The plasma concentration of LPS in HFD rats was slightly elevated compared to NFD rats. In conclusion, presented study indicates that gut dysbiosis in rats on a HFD may have a pro-inflammatory effect related to myocardial dysfunction.

*Acknowledgements*: This study was financially supported by statutory funds from the Medical University of Warsaw (1MA/N/2020).

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S6.L10

# EFFECTS OF PERIPHERAL CANNABINOID $CB_1$ RECEPTOR INVERSE AGONIST JD5037 IN MONO- AND POLYTHERAPY WITH METFORMIN IN A MONOCROTALINE-INDUCED RAT MODEL OF PULMONARY ARTERIAL HYPERTENSION

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Pulmonary arterial hypertension (PAH) is an incurable disease leading to an increased pressure in the pulmonary artery and right heart failure. It has been proved that the adenosine monophosphate-activated protein kinase (AMPK) activator, metformin (MET), plays a protective role in chronic PAH. Peripheral $CB_1$ receptor antagonists reduce the number of pathological changes in experimental lung fibrosis. The aim of this study was to evaluate the effect of the peripheral cannabinoid $CB_1$ inverse agonist JD5037 given in mono- or polytherapy with MET in an experimental PAH model and in PAH-free control animals. Experiments were performed on Wistar rats, in which PAH was induced by a single injection of monocrotaline (MCT) (60 mg/kg, s.c.) at day 0. The control group was injected with saline. During the experiment, which was conducted for 21 days, animals were given JD5037 (3 mg/kg), MET (100 mg/kg), combination of these compounds or its vehicles (DMSO, Tween, 0.9% NaCl or 0.9% NaCl, respectively) by oral gavage once a day. The MCT-induced PAH caused an increase in the right ventricular systolic pressure (RVSP), Fulton index (the right ventricle weight to left ventricle plus septum weight), lung hypertrophy and decrease of oxygen saturation. MET preventive treatment has shown a tendency to reverse these changes. JD5037 did not modify positively any of the parameters except for the tendency to increase the oxygen saturation. Polytherapy with JD5037 and MET has shown various changes. Not only did it tend to decrease right ventricle hypertrophy, but also caused a significant increase of the oxygen saturation and reduction of RVSP. In conclusion, the monotherapy with JD5037 does not influence PAH-related changes in physiological parameters significantly. However, the polypharmacological treatment with MET possesses better potency than any of these compounds alone.

Work financed under the project POWR.03.02.00-00-I051/16 from European Union funds, PO WER 2014-2020, grant No 10/IMSD/G/2019 and Medical University of Bialystok, grant No SUB/2/DN/21/002/2213.

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S6.L11

# HOW BEETROOT JUICE NITRATES CAN MODULATE THE FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM? A THEORETICAL FRAMEWORK

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According to the literature, beetroot juice contains a number of compounds that can have a significant impact on health, e.g. nitrates. Nitrates in the body are finally reduced to nitric oxide (NO), which has a positive effect on the cardiovascular system, inter alia, by regulating blood pressure. There are two ways of NO formation in the human body - the endogenous one using L-arginine and NO synthase (NOS) and the exogenous one using dietary nitrates, which are processed in the nitrate-nitrite-NO pathway. A frequently proposed mechanism of NO action in the circulatory system is a local effect leading to an improvement in blood flow by relaxing the blood vessels or by improving the function of the peripheral vascular endothelium. We have suggested that nitrogen oxide from beetroot juice may also improve cardiovascular parameters by modulating the autonomic nervous system (AUN), possibly influencing the reflex pathway, including the baroreceptor and peripheral chemoreceptor reflexes. In this presentation, we proposed a possible model for the effects of beetroot juice nitrates on AUN, pre-identifying possible challenges for scientists in this field.

*Acknowledgements*: This presentation was supported by the Ministry of Science and Higher Education 26 (Poland)/Wroclaw Medical University (The Young Scientist Project), Internal number: 27 STM.A090.20.108.

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S6.L12

# BREATHING DISORDERS IN ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a neurodegenerative, age-related disorder and most common reason for dementia, with over 45 million people worldwide affected. Its main features are cognitive and neuropsychiatric symptoms leading to progressive impairment and disability. The characteristic neuropathological abnormalities such as progressive accumulation of amyloid-β plaques (Aβ), intracellular neurofibrillary tangles of hyperphosphorylated tau protein, and decreased synaptic density are believed to result in neurodegeneration and depletion of brain neurotransmitters. Apart from impaired cognitive function, disturbances in respiration are a frequent occurrence in AD patients. Among them the leader is sleep apnea, but respiratory dysrhythmias, shortness of breath, bronchitis, and pneumonia are also observed. Despite serious respiratory problems that reduce quality of life, they are often undiagnosed and untreated and their causes are not well understood. There have been recent attempts to study respiratory changes in an animal model of disease induced by streptozotocin (STZ) injection into the lateral brain ventricles. Studies, imitating sporadic AD, showed significant astrogliosis in the commissural part of the nucleus tractus solitarii and blunted ventilatory response to hypoxia exposure (Ebel 2017, Brown 2019). Another study displayed only increased sensitivity to $CO_2$, attributed to augmented Aβ expression in the locus coeruleus (LC), an important chemosensitive area in the brainstem (Vincente, 2018). Unfortunately, the results differ despite fairly similar experimental conditions. In our study we investigated hypoxic and hypercapnic ventilatory responses in transgenic mice model of AD (AβPP V717I-'London mutation'). Transgenic mice with APP gene mutation and extensive AβPP overexpression recapitulate a number of features of familial early-onset AD cases. Our research displayed unchanged hypoxic ventilatory response and increased ventilatory response to hypercapnic stimulus. In further steps we examined whether treatments used in AD therapy have any impact on breathing. $APP^+$ mice were treated intraperitoneally with cholinesterase inhibitor-rivastigmine or NMDA receptor antagonist-memantine, in attempt to turn over augmented hypercapnic ventilatory response. Although memantine had no impact on respiration of $APP^+$ mice, rivastigmine was effective in reducing chemoreflex respiratory response due to decrease of tidal volume and frequency of breathing. Nevertheless, hypercapnic response did not return to the level present in control $APP^-$ mice suggesting that dysfunction of another neurotransmitter system may be involved in an altered response to hypercapnia, and this leaves room for further research.

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S6.L13

# DEFICIT OF MONOAMINES IN RESERPINE PARKINSON'S DISEASE MODEL ALTERS THE HYPOGLOSSAL NERVE ACTIVITY

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Hypoglossal (HG) and phrenic (PHR) nerves are the main nerves involved in respiratory muscle control. The respiratory deficits observed in Parkinson's disease (PD) may manifest as HG and PHR nerve dysfunction and may result not only from dopamine, but also serotonin and noradrenaline deficiencies. Therefore aim of this study was to analyze the activity of HG and PHR nerves in reserpine rat model imitating deficit of biogenic monoamines. Experiments were performed on anesthetized, paralyzed and vagotomized adult male Wistar rats divided into two groups; with reserpine 5 mg/kg and alpha-methyl-p-tyrosine 250 mg/kg pretreatment (n=7) and with vehicle injections (n=9). By the use bipolar electrodes the amplitude and frequency of discharges of both nerves in normoxia, acute hypoxia (8% $O_2$ in $N_2$) and during recovery after apnea were recorded. Following electrophysiological experiments brains were collected and striatum and brainstem were dissected to monoamine level detection by the HPLC analysis. Reserpine treated rats, in contrast to sham, showed decreased baseline amplitude and minute HG activity, and also blunted depressive phase after hypoxic exposition. The pre-inspiratory activity of HG nerve in reserpine treated rats was reduced by shortening the pre-inspiratory time of HG activity and the ratio of pre-inspiratory time to total respiratory cycle length and by decreasing the ratio of pre-inspiratory to inspiratory amplitude during normoxia, hypoxia and recovery. We suggest that the massive depletion in the brainstem of not only dopamine (75%), but also noradrenaline (92%) and serotonin (72%), has an impact on the pre-inspiratory activity of the HG. The pre-inspiratory HG activity is responsible for maintaining the appropriate diameter of the upper airway in the pre-inspiratory phase, preparing for inspiration. Altered pre-inspiratory activity in the reserpine rats may shed some light on the cause of obstructive sleep apnea development in some PD patients. New therapeutic strategy involving the supplementation of amine depletion other than dopamine is suggested.

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S6.L14

# DAILY SITTING TIME AFFECTS LACTULOSE-INDUCED CHANGES IN HYPOXIC RESPONSIVENESS IN HUMANS

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Despite growing interest in the role of gut microbial signaling in the regulation of multiple physiological systems, our understanding of the contribution of gut microbiota to respiratory control in humans remains very limited. We have recently demonstrated in a group of healthy subjects that the increased gut microbial fermentation is associated with augmented ventilatory responses to transient hypoxia, which implied the altered function of peripheral chemoreceptors. In this report, we have evaluated whether such changes in hypoxic responsiveness might be related to the subjects' body composition and declared physical activity. Sixteen healthy volunteers (8 men; mean ± SD age 25.9 ± 5.2 years) underwent two separate trials, receiving lactulose (stimulating gut microbial fermentation) or placebo. Ventilatory and haemodynamic responses to the acute hypoxia were evaluated before and two hours after the test meal. Hydrogen breath tests were applied to evaluate gut fermentation intensity. All participants underwent anthropometric measurements and body composition analysis, and filled IPAQ-SF questionnaire. Declared sitting time (ST; hours per day) negatively correlated with the magnitude of the lactulose-induced changes in the following hypoxic responses: minute ventilation response ($r= –0.57$, $p=0.022$); heart rate response ($r= –0.64$, $p=0.007$); systemic vascular resistance response ($r= –0.69$, $p=0.005$). No such correlations were obtained in placebo test. Neither ST, nor aforementioned changes in hypoxic responses were found related to the body composition parameters (BMI, body fat content, skinfold thicknesses; $p >0.05$). Daily sitting time modulates the effect of increased gut microbial fermentation on the hypoxic responsiveness in humans. These results emphasize the need of further research linking gut microbiome, physical activity and respiratory control mechanisms.

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S6.L15

# VASOPRESSIN AND V1A RECEPTORS IN HEMODYNAMIC AND RESPIRATORY REGULATION IN NORMOTENSIVE AND HYPERTENSIVE RATS

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Vasopressin (AVP) and its V1a receptor (V1aR) have been implicated in pathophysiology of essential hypertension. V1aRs have been found in the cardiovascular and respiratory neurons of the brainstem and in the carotid bodies. AVP has been shown to affect both circulatory and respiratory function in normotensive animals. In our study we investigated the role of AVP and V1aRs in the regulation of cardiorespiratory parameters under normo- and hypertensive conditions. Male normotensive Wistar-Kyoto (WKY) (n=7) and spontaneously hypertensive (SHR) (n=7) rats were instrumented with: vascular catheters implanted into the femoral vein (intravenous (i.v.) infusions) and the femoral artery (hemodynamic parameters); the tracheal tube (respiratory parameters); and subcutaneous ECG electrodes (heart rate; HR). The responses to AVP (10 ng/100 µL i.v.) and pharmacologically evoked arterial chemoreflex (KCN; 30 microg/100 microL i.v.) were tested before and after administration of V1aR antagonist ((d(CH2)51,Tyr(Me)2,Arg8)-vasopressin; 5 µg/100 µL i.v.). Resting mean arterial blood pressure (MABP) and minute ventilation (MV) were significantly higher and the chemoreflex-evoked changes of MABP and MV were significantly greater in SHR than in WKY rats. In SHR rats administration of AVP resulted in a significantly greater increase in MABP than in WKY controls, but only in SHR it was accompanied by reduction in MV and respiratory rate (RR). Blockade of V1aRs caused a decrease of MABP in both groups and increase in MV and RR only in SHR rats. V1aR antagonist decreased the pressor response of the chemoreflex and abolished all responses to AVP in both groups. Our findings confirm increased sensitivity of the arterial chemoreflex and enhanced pressor and respiratory responses to AVP in SHR rats that are dependent on V1aRs.

*Acknowledgements*: This work was supported by the Polish Ministry of Science and Higher Education (grant No. DI2018 020648).

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S6.P1

# CHEMOSENSITIVITY DURING MECHANO AND METABOREFLEX ACTIVATION IN HEALTHY SUBJECTS CHARACTERIZED BY LOW AND HIGH EXERCISE CAPACITY

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The behavior of the peripheral chemoreceptor reflex during: (i) concomitant stimulation of the muscle mechanoreceptors alone, or (ii) combined stimulation of mechano- and metaboreceptors remains poorly known and the nature of the interaction between these reflexive mechanisms is likely to be influenced by the level of aerobic and/or anaerobic capacity. This study aimed to explore this issue in a group of 19 healthy, young volunteers: 9 men; age: 28.5 ± 3.8 years, body mass index: 24.0 ± 3.7 kg/m2 (mean ± SD). Anaerobic fitness was tested by the Wingate test, while aerobic fitness was tested with the progressive RAMP test. A bicycle ergometer was used for both tests. Peripheral chemoreflex sensitivity (PChS) was assessed by the transient hypoxia method at rest, during passive pedaling (activation of muscle mechanoreflex), and passive pedaling with circulatory occlusion of the lower limbs (simultaneous activation of muscle mechano- and metaboreflex). The subjects were divided into the low- and high-anaerobic fitness groups and the low- and high-aerobic fitness groups according to medians of the Wingate test and the RAMP test, respectively, and the PChS at rest, during passive pedaling and passive pedaling with circulatory occlusion of the lower limbs were compared between low- vs. high-fitness groups. We found no difference in the PChS at rest, during passive pedaling and passive pedaling with circulatory occlusion of the lower limbs between the high- and low-fitness groups. It can be concluded that the level of the aerobic and anaerobic capacity does not affect the nature of the interaction between the peripheral chemoreflex and the mechano- and metaboreflexes in humans.

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S6.P2

# CARDIAC PHYSIOLOGY AFTER OSTARINE TREATMENT – *IN VITRO* STUDY ON H9C2 CARDIOMYOCYTES AND FIBROBLASTS

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Selective androgen receptor modulators (SARMs) are a dynamically developing group of anabolic substances. While many SARMs have been tested in clinical trials, none have been yet approved by the drug committee (FDA). The most popular of them is ostarine (enobosarm, GTx-024), a compound that is becoming more and more popular as a doping agent, using often in high doses. Easy access and interest in these compounds means that the actual number of SARMs users is large and steadily growing. The dangerous effects of anabolic androgenic steroids (AAS) on the heart are being investigated - i.e. myocyte hypertrophy, disturbation in the lipid profile or promote fibrotic changes have been described. However, ostarine has not been studied for its effects on the heart. We decided to investigate the effect of ostarine on the metabolism and functioning of the heart using *in vitro* techniques. H9C2 myoblast lines and isolated fibroblasts from the hearts (CF) of young rats were used. Cells were treated with ostarine at selected doses for 24 and 48 hours, then we determined protein content, survival and proliferation using MTT and BrdU. Additionally, CF were treated for 24, 48 and 72 h to assess the expression of the fibrosis genes. We have shown that ostarine affects cell proliferation, survival, and protein content in tested cells. We also showed an increase of gene expression - fibronectin and αSMA involved in the processes of fibrosis. According to our results, ostarine may have a negative impact on the functioning of the heart. The use of ostarine may be a potential risk factor in the development of cardiovascular disease, but more research is needed.

*Funding*: The work was financed by the Polish Ministry of Science and Higher Education (project number 2019/35/N/NZ7/00738).

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S6.P3

# EVALUATION OF THE ANTI-INFLAMMATORY AND ANTI-PROLIFERATIVE PROPERTIES OF CANNABIDIOL IN AN EXPERIMENTAL MODEL OF MONOCROTALIN-INDUCED PULMONARY HYPERTENSION.

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Pulmonary hypertension (PH) is a rare disease of multifactorial etiology leading to right ventricular failure and remodeling of pulmonary arteries of small diameter (40–100 μm). Additionally, in development of PH inflammatory process is involved and level of inflammatory mediators positively correlates with the advancement of the disease. Cannabidiol (CBD), isolated from *Cannabis sativa* L. var. *indica*, is characterized by a lacks of psychoactive properties and its potential therapeutic use in diseases related to inflammation and proliferation has been suggested. The aim of the study was to evaluate the effect of CBD on the selected parameters of inflammation and remodeling in the lungs of rats with PH induced with the plant alkaloid - monocrotaline (MCT) - MCT-PH rats. The studies were carried out on rats with and without PH (control group). CBD (10 mg/kg) or its solvent was administered in a preventive model, once daily intraperitoneally for 3 weeks (from day 1 to 21) after administration of MCT at a dose of 60 mg/kg (in groups with MCT-PH) or solvent for MCT (in groups without PH). ELISA, western blot and immunohistochemistry methods were used. A very strong expression of galectin-3, a marker of inappropriate pulmonary remodeling and inflammation, was found in the lungs of rats with MCT-PH and the alveolar macrophages of these rats showed morphological signs of activation. MCT-PH group showed increased concentration of inflammatory parameters in lung tissue (tumor necrosis factor-α and nuclear factor-κB) and serum (M-CSF). Administration of CBD to MCT-PH rats resulted in a marked reduction of galectin-3 and interleukin-1 immunoreactivity, and inflammatory mediators. In conclusion, CBD could be used as an adjunct therapy in the treatment of PH because of its potential property of stopping or slowing down the remodeling process caused e.g. by inflammation, and thus limiting the adverse effects of the development of PH.

*Acknowledgements*: Supported by grants of the Medical University of Bialystok: SUB1/DN/21/001/2213, SUB2/DN/21/003/2213.

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S6.P4

## THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS ANACETRAPIB AND TORCETRAPIB ON LIVER DIMETHYLARGININE DIMETHYLAMINOHYDROLASE-1 ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA

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Dimethylarginine dimethylaminohydrolase (DDAH) is an enzyme found in all mammalian cells. There are two isoforms of DDAH - DDAH1 and DDAH2, with some differences in tissue distribution of the two isoforms. DDAH1 predominates in tissues that express neuronal NOS (nitric oxide synthases), while DDAH II predominates in tissues expressing endothelial NOS. DDAH degrades methylarginines, specifically asymmetric dimethylarginine (ADMA) and NG-monomethyl-L-arginine (MMA). Inhibition of DDAH activity causes methylarginines to accumulate, blocking nitric oxide(NO) synthesis and causing vasoconstriction. An impairment of DDAH activity appears to be involved in the elevation of plasma ADMA, and impairment of vascular relaxation observed in humans with cardiovascular disease or risk factors. The activity of DDAH is impaired by oxidative stress. The cholesteryl ester transfer protein (CETP) inhibitors have ability to elevate high density lipoprotein (HDL) level. It is supposed that protective effect of CETP inhibitors on endothelial function may be HDL-independent and related to its effect on DDAH/ADMA/NO pathway. The present study was undertaken in order to answer the question whether the treatment of anacetrapib or torcetrapib affect liver DDAH1 activity/expression and therefore modulate endothelial function. Fructose-induced (FRU) dyslipidemic rats were treated for 1 week with anacetrapib (ANA) (3.0 mg/kg p.o) or with torcetrapib (TOR) (10 mg/kg, p.o). Liver activity of DDAH1 and plasma NO concentration were measured spectrophotometrically. The expression of DDAH1 protein was determined by ELISA method. The administration of both drugs increased plasma NO level in fructose-fed rats. Both ANA and TOR had no effect on liver DDAH1 activity. The significant increase of DDAH1 expression was found in liver of fructose-fed rats treated with torcetrapib (FRU+TOR) vs. fructose-fed rats (FRU) and fructose-fed rats treated with anacetrapib (FRU+ANA). We concluded that treatment with CETP inhibitors increased plasma NO level and affected DDAH1 expression in rats' liver. Therefore, treatment with CETPi most probably modulate endothelial function in dyslipidemia.

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S6.P5

## THE CHARACTERISTICS OF A SUB-CHRONIC MODEL OF NON-ATOPIC ASTHMA

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Non-atopic asthma is, contrary to the allergy-related form of the disease, more severe and more difficult in treatment, less responsive to corticosteroids, and involves neutrophils instead of eosinophils in its progression. There are only a few animal models of the disease, none of them being proven to be chronic. Therefore, there is a high need for stable models of non-atopic asthma enabling a chronic or sub-chronic administration of potential drugs. The aim of the study was a verification if the hapten-induced murine model of asthma remains stable for at least two weeks after final induction. For this purpose, adult Balb/c mice were twice skin-sensitized with DNFB, and 4 days later were challenged intratracheally with DNS. A methacholine test was performed to access the airway hyperreactivity. Later, the animals were kept for two weeks in the local animal facility under standard conditions. Then, the mice were once again challenged with DNS and the methacholine test was repeated. At the end, the number of inflammatory cells in BALF was determined. Control recordings showed a typical pattern of airway hyperreactivity (AHR) in non-atopic asthma with growing PenH values in response to increasing methacholine concentrations. After two weeks, the pattern of AHR changed and the reaction to methacholine was weaker at its higher concentrations. Parallelly, basic ventilatory parameters including ventilation, breathing frequency, and inspiratory/expiratory times did not change. The total number of inflammatory cells increased while the percentage of neutrophils declined compared to single DNS challenge mice. The results suggest a decrease of airway hyperreactivity, a stabilization of the airway inflammation at the level of cellular influx and a probable shift towards other forms of asthma, the non-neutrophilic ones. This leads to the conclusion that the DNFB/DNS-induced model of non-atopic asthma is not stable during two weeks after induction. To maintain the proper level of features of non-atopic asthma, a re-sensitization repeated each week should be considered.

*Acknowledgements*: This research was partially supported by the Polish National Research Centre, *MINIATURA* research grant 2017/01/X/NZ5/00325.

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S6.P6

## THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS, ANACETRAPIB AND TORCETRAPIB, ON PLASMA AND LIVER PARAOXONASE 1 (PON 1) ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA

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The paraoxonase family consists of three proteins: PON1, PON2 and PON3. They are differentially expressed and have different functions. PON1 is an antioxidant glycoprotein synthesized in the liver and secreted to the bloodstream. It binds high-density lipoproteins (HDL) and therefore potentiates their antioxidant and antiatherogenic properties. The cholesteryl ester transfer protein (CETP) inhibitors are a new class of lipid-lowering drugs that can elevate HDL level. However, the development of various cardiovascular diseases is related to HDL function, rather than HDL level. The present study was undertaken in order to answer the question whether the treatment of anacetrapib or torcetrapib can modulate PON1 activity and expression, the HDL-associated antioxidant enzyme. Fructose-induced (FRU) dyslipidemic rats were treated for 1 week with anacetrapib (ANA) (3.0 mg/kg p.o) or with torcetrapib (TOR) (10 mg/kg, p.o). Plasma and liver activity of PON1 was measured spectrophotometrically. PON1 protein expression was assessed by enzyme immunoassay technique. Eight 8 weeks of fructose administration resulted in decrease of plasma PON1 activity. By contrast, the significant increase of PON1 activity was found in the liver of fructose-fed rats (FRU). The treatment with anacetrapib and torcetrapib resulted in the significant reduction in PON1 activity in the liver. Moreover, TOR increased the PON1 expression in the liver. Both drugs did not affect PON1 plasma PON1 activity and concentration. We conclude CETP inhibitors can impact PON1 activity and expression in the liver but they had no effect on and HDL antioxidant function.

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S6.P7

## LONG-TERM EFFECT OF PERIPARTUM DEPRESSION ON THE CARDIOVASCULAR SYSTEM OBSERVED IN THE ADULT RAT FEMALE OFFSPRING

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Peripartum depression is a significant clinical problem affecting both the mother and her offspring. We have previously reported that maternal depression results in altered neurodevelopment and cardio development when examined in adolescent (35-day-old) rat offspring evidenced by significantly increased heart rate and left ventricular (LV) diastolic dysfunction. The present study examined the possibility that the effect of peripartum depression on the cardiovascular system may persist until adulthood. The study was carried out on 14 Sprague Dawley rat dams and their offspring. Half of the dams underwent chronic immobilization stress to induce depression. A urinary corticosterone concentration confirmed immobilization-induced development of the depressive state in dams. The effect of peripartum depression was measured in depressed female offspring (DO) and control females offspring (CO) at six months of age in terms of blood pressure and heart functions (ECHO). Maternal peripartum depression did not significantly affect body weight and LV weight of the offspring. The DO offspring had significantly higher values of both systolic and diastolic blood pressure compared to the CO offspring. ECHO analysis revealed mild LV hypertrophy in the DO offspring. The interventricular septum thickness at end-diastole (IVSd) and LV posterior wall thickness at end-diastole (LVPWd) were both increased in the DO offspring compared to CO offspring. Additionally, LV diastolic dysfunction suggested by the decrease in the speed of the wave e' and the increased ratio of E/e' was observed in the DO offspring. These results suggest that peripartum depression can have a long-term effect on the cardiovascular system persisting until adulthood.

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S6.P8

# ELECTROPHYSIOLOGICAL, HEART RATE VARIABILITY, AND BIOCHEMICAL DISTURBANCES IN A RAT MODEL OF 5-FLUOROURACIL INDUCED CARDIOTOXICITY ARE PARTIALLY REVERSED BY CHRONIC VITAMIN D SUPPLEMENTATION

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5-fluorouracil (5-FU) is the most commonly used drug belonging to the fluoropyrimidines. Disturbances of cardiac muscle are one of the most common and dangerous side effects of fluoropyrimidines, including: chest pain, arrhythmias, heart failure, and myocardial infarction. Cardiovascular complications most commonly occur during the first dose. The aim of the study was to evaluate electrophysiological, heart rate variability (HRV), and biochemical changes observed after subsequent doses of 5-fluorouracil and after attempting to reduce cardiotoxicity using vitamin D supplementation. 60 adult male Wistar rats were included in the study. The rats were randomized into 4 groups: in group 1, the rats received 0.9% saline p.o. daily; in group 2, the rats received vitamin D (500 IU/kg) p.o. daily; in group 3, the rats received up to 4 doses of a 0.9% saline i.p. injection every two weeks with 0.9% saline p.o. daily; in group 4, the rats received up to 4 doses of 5-FU (150 mg/kg) i.p. every two weeks with vitamin D (500 IU/kg) p.o. daily. The first injection of 5-FU decreased mean heart rate (289 vs. 275 (beats/min)), sBP (119 vs. 103 (mmHg)), and increased both SDNN (3.22 vs. 4.08 (ms)) and the HRV triangular index (1.51 vs. 1.72). Vitamin D supplementation partially reverse these changes. ECG parameters were affected, including QRSt (34.4 vs. 40.1 (ms)) and QTt (55.8 vs. 62.1 (ms)). Biochemical parameters and ELISA revealed increases in troponin levels after the first and fourth dose (6.65 and 11.92 (ng/ml), respectively). Conclusions: Both electrophysiological and heart rate variability disturbances were observed after subsequent 5-FU administrations, predominantly after the first dose of 5-FU. Chronic vitamin D supplementation reduced partially these cardiotoxic effects of 5-FU in rat model.

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S6.P9

# TUMOUR NECROSIS FACTOR RECEPTORS TYPE 1 AND TYPE 2 ARE EXPRESSED IN THE BRAINSTEMS OF NORMOTENSIVE AND HYPERTENSIVE RATS

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Tumor necrosis factor (TNF) is a pleiotropic cytokine involved in the regulation of the cardiovascular system. Accumulating evidence indicates that increased levels of TNF in the brain are associated with arterial hypertension. Proinflammatory effects of the cytokine are mediated by TNF type 1 receptors (TNFR1), whereas activation of TNF type 2 receptor (TNFR2) exerts anti-inflammatory actions. The evidence of expression of both receptors in the cardiovascular centres of the brainstem is limited. We seeked to determine the expression of TNF receptors in the brain regions encompassing cardiovascular centres in normo- and hypertensive rats. In normotensive Wistar-Kyoto (WKY) (n=6) and in spontaneously hypertensive (SHR) (n=6) rats systolic blood pressure (SBP) was measured with tail-cuff method and brains were harvested. Expression of TNFR1 and TNFR2 mRNA was evaluated with RT-PCR in the dorsal and ventral aspects of the medulla containing respectively NTS and RVLM and in the hypothalamus. Immunostaining of TNFR1 and TNFR2 in the brainstem and in the hypothalamus was carried out in WKY and SHR rats (n=2). SHR rats had significantly higher SBP than WKY controls. There were no significant differences in the mRNA expression of TNFR1 and of TNFR2 in the investigated regions between SHR and WKY rats. Immunostaining revealed presence of both subtypes of TNF receptors in the brainstem and in the hypothalamus in both groups. TNF type 1 and type 2 receptors are expressed in the central nervous system, however, surprisingly mRNA levels of the receptors are similar between normotensive WKY and hypertensive SHR rats.

*Acknowledgements*: The study was supported by the Medical University of Warsaw, grant no. 1MA/NM2/18/18.

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S6.P10

# DEVELOPMENT OF HEART FAILURE IN SPONTANEOUSLY HYPERTENSIVE RATS

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Spontaneously hypertensive rats (SHR) rats are an animal model that strictly reflects to the one of the most common cardiovascular diseases in humans- hypertension. SHR rats are characterized by the development of spontaneous arterial hypertension from 5-6 weeks of age. This study aimed to test whether SHR rats will develop heart failure based on long-term hypertension. Rats were housed in a conventional animal facility with a 12/12 h day/night cycle, in a room with stabilized temperature and humidity (22 ± 2°C, 55 ± 10% humidity). Wistar Kyoto (WKY) rats were the control group, the test group was SHR rats. The studies were conducted after the rats were 6-, 12- and 18-month-old (n=5 in each group). Rats were anesthetized with ketamine (20 mg/kg) and xylazine (10 mg/kg) intraperitoneally. After chest hair removal, animals were placed on a heated platform to maintain the body temperature at 37°C. Transthoracic echocardiography was performed on each animal using a Vevo 1100 (VisualSonics Inc, Canada) equipped with a 40 MHz linear transducer. Images were obtained at a frame rate consistently above 200 frames/s. The transducer was placed above the anterior chest wall. The obtained acquired images were used to calculate hemodynamic parameters such as systolic volume (V systol), diastolic volume (V diastol), stroke volume (SV), LV ejection fraction (EF), and fractional shortening (FS) as well as cardiac output (CO). To measure blood pressure parameters, such as systolic, diastolic, and mean blood pressure, likewise heart rate the CODA tail-cuff system was used. The statistical analysis was performed using Graph Pad Prism 8 (Graph Pad Software). Paired Student t-test was used for comparisons between two groups. Results are presented as mean ± SEM. Based on a statistical analysis of hemodynamic parameters, changes in heart function in SHR rats over time were observed. Left ventricular systolic dysfunction was not observed based on the ejection fraction (EF) in 6-month-old SHR rats (74.26 ± 4.34 vs. 70.32 ± 2.88 (%])). However, in the group of 12-month-old SHR rats, a statistical decrease of this parameter was observed compared to the WKY group (68.86 ± 3.17 vs. 78.73 ± 1.97 (%)). Moreover, in a group of 18-month-old rats, this occurrence was even more pronounced (61.83 ± 1.3 vs. 75.29 ± 2.24 (%)). Another important parameter describing the systolic function of the left ventricle is fractional shortening (FS). The deterioration trend of left ventricular function based on FS was the same as in the of EF (WKY vs. SHR: 6-month: 45.02 ± 3.02 vs. 39.73 ± 2.17; 12-month: 47.36 ± 1.81 vs. 39.06 ± 2.48; 18-month: 44.21 ± 2.16 vs. 32.99 ± 0.85 (%)). All examined SHR rats developed advanced arterial hypertension (systolic/diastolic BP: 198 ± 5.83/145 ± 7.8 (mm Hg); heart rate: 354 ± 11.37 (bpm)). The presented results indicate the development of left ventricular heart failure based on long-term hypertension in SHR rats. This allows the SHR model to be used in experimental *in-vivo* studies in the field of heart failure.

*Acknowledgements*: HARMONIA 2016/22/M/NZ4/00678.

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S6.P11

# STEAROYL-COA DESATURASE 4 DEFICIENCY PROTECTS AGAINST HIGH FAT DIET-INDUCED HEART DYSFUNCTION IN MOUSE

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Stearoyl-CoA desaturase (SCD) is an enzyme involved in biosynthesis of monounsaturated fatty acids, what was shown as a crucial point in the regulation of cardiac metabolism. SCD4 is expressed exclusively in the heart and its expression is significantly increased after a high-fat diet (HFD). Therefore, the aim of the present study was to determine the impact of SCD4 deletion on heart function in HFD induced steatosis. Our study showed that HFD in wild type (WT) mice led to remodeling of left ventricle by increased relative wall thickness, decreased end-diastole diameter and stroke volume, but also reduced cardiac output. Simultaneously, no changes in cardiac structure and function were observed in $SCD4^{-/-}$ mice after HFD. Additionally, no changes in expression of hypertrophy markers i.e. α- and β-myosin heavy chain, was observed after HFD in both genotypes. Interestingly, brain natriuretic peptide expression (peptide hormone involved in inhibition of fibrosis, hypertrophy and cardiac steatosis) was decreased in WT hearts after HFD. In $SCD4^{-/-}$ mice this effect was not observed, suggesting beneficial effect of SCD4 deficiency on heart function after HFD. Furthermore, in WT mice in contrast to $SCD4^{-/-}$ proteins involved in Ca2+ dependent cardiac contractility control like $Ca^{2+}$/calmodulin-dependent protein kinase II and sarcoplasmic reticulum $Ca^{2+}$-ATPase 2 were decreased and phospholamban was increased after HFD. These changes are consistent with decreased stroke volume noticed only in WT HFD mice. Summarizing, obtained results show that SCD4 is an important point in regulation of heart function and SCD4 is involved in control of induced by HFD changes at morphological and molecular levels in the heart.

*Funding*: This work was supported by grant from the National Science Centre, Poland (no. UMO-2016/22/E/NZ4/00650).

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S6.P12

## ASSOCIATION BETWEEN DEPRESSION AND UNFAVORABLE NUTRITIONAL, CARDIAC AND LABORATORY OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE

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To date, there are no literature reports combining the relationship between depression and chronic heart failure (CHF) in relations to selective nutritional, cardiac and laboratory parameters. The aim of this study was to assess how depression condition in CHF parameters reflects nutritional and laboratory parameters in comparison with non-depressive patients. We enrolled 94 CHF individuals to assess depression prevalence and to compare values of cardiac, laboratory and nutritional parameters between depressed and non-depressed patients. Depression was diagnosed in 66 individuals (70.2%). We noted significant reduction of EF% in group of depressive patients compared to disease-free individuals (mean EF%: 42 ± 12 and 49 ± 9; p=0.030) and worse outcomes in NYHA examination (p <0.001). Depressed patients demonstrated lower body weight (p=0.023), BMI (p=0.044), serum albumin concentration (p=0.015), hemoglobin concentration (p=0.042) and elevated level of CRP (p=0.025) in contrast to non-depressed group. Moderate or severely depressed group demonstrated decreased level of EF% (p=0.019) and increased LAD (p=0.040) comparing with group suffering from mild depression. We observed greater susceptibility to develop cachexia in patients diagnosed as moderately or severely depressed (p=0.030). Moreover, in the mentioned group of patients, the lower values of body weight (p=0.037), FFM (p=0.022) and hemoglobin concentration (p=0.007) was found. Depression in CHF patients is associated with worse cardiac, laboratory and nutritional outcomes. Unfavorable clinical characteristics of CHF patients is related to depression severity.

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S6.P13

## RELATION BETWEEN THE HEART RHYTHM ASYMMETRY AND THE RESPIRATORY PHASE IN HEALTHY PEOPLE AND PATIENTS WITH ARTERIAL HYPERTENSION

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Heart rate asymmetry (HRA) is a physiological phenomenon in a healthy subject. We used Guzik's Index (GI) and Porta's Index (PI) to assess HRA in healthy subjects and patients with hypertension. All subjects were examined in a supine position, and 20-minute recordings of ECG and respiration were obtained. In the following, we analyse data from 18 healthy adults (CG: age: 45 ± 14) and 19 patients with hypertension (HG; age: 53 ± 13) who had regular breathing pattern. For each patient, we assign RR-intervals to one of four states corresponding to the phase of breathing: inspiration (IN) or expiration (EX), and two possible breathing phase transitions: from inspiration to expiration (IN›EX) or from expiration to inspiration (EX›IN). Poincare plots for pairs of RR-intervals from subsequent respiratory phases for both groups were obtained. Then the HRA was estimated by the two indices (GI and PI). Both indices estimate the distribution of the points concerning the line of identity. In standard assessment (without considering respiratory phase), GI tended to be different in healthy subjects and hypertensive patients (p <0.07), and the value of GI for healthy subjects was significantly different from 50% (p <0.005), which means that asymmetry has been found in the CG. Nonetheless, the asymmetry of RR-intervals was not detected by PI. At the same time, values of asymmetry indices (GI and PI) obtained from RR-intervals in various respiratory phases were statistically different. Although, in this kind of analysis CG and HG groups presented similar characteristics.

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S6.14

# POST-EXERCISE HYPOTENSION IN ELDERLY: THE EFFECT OF SINGLE SESSION OF WATER BASED EXERCISE

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Among cardiovascular diseases, hypertension has been considered with high prevalence. In this way, countless treatments are often attributed as disease management strategies, in this way, the physical activity is highlighted above all for being able to reduce blood pressure. However, the hypotensive effect in acute sessions performed in an aquatic environment still remains inconclusive. Thus, the objective of the study was to verify the hypotensive effect of a water based exercise in normotensive and hypertensive elderly people. Twenty eight physically independent elderly women were distributed in two groups being normotensive (N, n: 10) and hypertensive of stage 1 (H, n: 18). All subjects were submitted to single session of 45-minute of water based exercise session, consisting of 5 minutes of warm-up, 35 minutes of the main part and 5 minutes of calm down. The intensity was monitored by the subjective perception of effort, indicating that throughout the main part the exercises were performed between 6 and 7 on the 0-10 scale. The following parameters were analyzed before and after 60 minutes of the exercise session: systolic (SBP), diastolic (DBP) and mean (MBP) blood pressure, heart rate (HR) and rate pressure product (RPP). Differences were analyzed by t test or ANOVA repeated measures as appropriate and significance level of $p < 0.05$. No significant differences ($p > 0.05$) were found between age and anthropometric parameters between groups N and H. No differences were found in both groups in HR ($F=0.194$, $p=0.66$), SBP ($F=1.685$, $p=0.20$), DBP ($F=2.52$, $p=0.125$), MAP ($F=1.54$, $p=0.22$) and SD ($F=2.02$, $p=0.16$) after immersion. Analyzing the hypotensive response induced by the exercise session, a significant effect was found in SBP (time: $F=12.74$, $p=0.001$; group: $F=77.96$, $p<0.001$; interaction: $F=7.25$, $p=0.012$), MBP (time: $F=11.09$, $p=0.002$; group: $F=118.7$, $p<0.001$) and RPP (time: $F=9.65$, $p=0.004$; group: $F=22$, 05, $p<0.001$; interaction: $F=4.52$, $p=0.043$). Thus, 60 minutes after the exercise session, significant reductions ($p<0.05$) were found in the SBP (N: –1.6 ± 3.48, H: –9.57 ± 8.96;%), DBP (N: 0.98 ± 3.09, H: –3.10 ± 5.59;%), MBP (N: –1.26 ± 2.10, H: –4.37 ± 5.00; %) and RPP (N: –2.28 ± 3.71, H: –11.27 ± 12.29;%). Conclusion: an acute session of water based exercise was able to promote a reduction in systolic, diastolic and mean and rate pressure product in hypertensive elderly women.

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S6.P15

# THE EFFECTS OF ENHANCED ENDOCANNABINOID TONE INDUCED BY CHRONIC ADMINISTRATION OF DUAL FAAH/MAGL INHIBITOR JZL195 IN SPONTANOUSLY HYPERTENSIVE RATS

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Two major endocannabinoid degrading enzymes are fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL). We have previously demonstrated that chronic administration of FAAH inhibitor induced different (also positive) age- and model-dependent effects on various cardiovascular system in normotensive and hypertensive rats. The therapeutic potential of stronger enhancement of endocannabinoid tone by dual FAAH/MAGL blockade in hypertension is unknown. Thus, the aim of our study was to examine the influence of dual FAAH/MAGL inhibitor JZL195 on the cardiovascular system in spontaneously hypertensive rats (SHR). Experiments were performed on 8–11 weeks old SHR and their appropriate normotensive control Wistar Kyoto rats (WKY). JZL195 10 mg/kg or its vehicle were injected intraperitoneally once daily for two weeks. Blood pressure (BP) and heart rate (HR) were measured in conscious animals using the tail-cuff method. Blood glucose in tail capillary blood, rectal temperature and organ weight (expressed as organ weight to body mass or tibia length ratio) were measured at the end of experiments. Systolic, mean and diastolic BP and HR measured before the first injection of JZL195 was higher in SHR than in WKY. JZL195 tended to decrease BP slightly (in SHR but not in WKY) and did not affect HR. Hypertensive rats had cardiac hypertrophy, lower body mass and kidney weight (but only expressed as tibia length ratio), comparable rectal temperature and lung and liver weight in comparison to normotensive animals. JZL195 did not affect any of these parameter. In conclusion, chronic administration of JZL195 did not exhibit significant benefit influences (but also did not evoke adverse effects) in hypertension, so further investigations are necessary to determine its real antihypertensive potential.

*Acknowledgements*: The work was supported by the National Science Centre, Poland, research grant No. 2016/21/N/NZ7/02338.

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S6.P16

## EFFECT OF MUSIC ON TRAINING PARAMETERS AND MOOD STATE IN HIIT BODY WORK SESSIONS

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Use of music in exercise sessions has been considered an interesting strategy for both psychophysical and psychophysiological effects. However, considering the high intensity interval training (HIIT), the effects of music remain inconclusive. In this way, the objective of the study was to evaluate the influence of music in HIIT sessions using body weight (HIIT-C) in internal training load parameters and in the mood of university students. Eight physically healthy and independent men were randomly submitted to three sessions of HIIT-C with the influence of song they like (SL), dislikes (DL) and without music (WM). The HIIT body weight session consisted of 20 sets of 30 s stimulus with all-out intensity and 30 s of passive recovery using the following exercises: jumping jack, burpee, mountain climber and squat jump. The following parameters were analyzed: heart rate (HR), lactate (La), number of movements (NM), perceived exertion (PE), perception of pleasure (PP) and the state of humor (BRUMS). Differences were analyzed by ANOVA-two-way with a significance level of $p<0.05$. Results: Although an increase ($p<0.05$) in HR, La and PE was found after the HIIT-C session, no difference was found in HR (WM: 167.83 ± 6.96; DL: 168.66 ± 11.67; SL: 163.33 ± 15.59 bpm; F=0.33; p=0.724), La (WM: 14.38 ± 3.11; DL: 16.01 ± 3.77; SL: 15.70 ± 3.20 $mMol.L^{-1}$; F=0.32; p=0.730) and PE between exercise sessions. Condition SL promoted greater (F=18.83; p=0.001) NM compared to DL and WM which also differed from each other. Considering the PP, the effect of music was found between the protocols (F=26.07; p=0.0001) indicating that the SL session promoted an increase in pleasure, different from the DL session that caused displeasure and the WM that did not promote modification. According to the Brunel mood scale, the feeling of fatigue was increased after HIIT-C (F=15.79; p=0.0054) with no difference between sessions, the WM condition and SL were able to decrease the sensation of tension after exercise. Increases in the parameter of mood disorder were observed both for the condition WM and DL, while the SL did not have a significant effect Conclusion: HIIT-C sessions using SL presented a higher NM and positive PP when compared to sessions with DL and WM without promoting changes in internal training load parameters. Although all sessions of HIIT-C increased the feeling of fatigue, the sessions of HIIT-C that use SL and WM showed less tension when compared to the session with DL. In addition, the WM and DL sessions were able to increase the mood disorder, with no effect for the SL session.

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S6.P17

## THE EFFECT OF GENETICALLY ALTERED AMP DEAMINASE ACTIVITY IN EXPERIMENTAL ISOPROTERENOL-INDUCED HEART FAILURE

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Studies on the influence of AMP deaminase (AMPD) activity on the progression of heart disease are conflicting, possibly due to the diverse effect in different clinical conditions. Isoproterenol is a non-selective β-adrenergic agonist that has been used widely to mimic the heart failure state. Our study aims to investigate the effect of isoproterenol (ISO)- induced heart failure on cardiac function in murine hearts lacking AMPD3. In this study we used male wild type and AMPD3 knockout mice (n=6–8). We injected intra-peritoneally ISO in the experimental animals at a dose of 100 mg/kg body weight/day for 12 days. ISO-treated and control mice (saline) from each group were examined with echocardiography. At the age of 12 months old, mice were anesthetized intraperitoneally with ketamine (100 mg/kg) and xylazine (10 mg/kg). After chest hair removal, animals were placed on a heated platform to maintain the body temperature at 37°C. The transthoracic echocardiography was performed using the Vevo 1100 (VisualSonics Inc, Canada) equipped with a 40-MHz linear array transducer. Images were acquired at a frame rate consistently above 200 frames/s. The transducer was placed above the anterior chest wall and hemodynamic parameters, including stroke volume (SV), left ventricular (LV) ejection fraction (EF) and fractional shortening (FS) as well as cardiac output (CO) and LV mass were collected. The statistical analysis was performed using Graph Pad Prism 7 (Graph Pad Software). Paired Student t-test was used for comparisons between two groups. A p-value <0.05 was considered as a significant difference. To characterize the implications of the AMPD KO for the ISO-induced development of cardiac dysfunction, we conducted two-dimensional echocardiographic measurements. The measurement of SV and CO did not differ in the studied groups, both WT and AMPD KO and after the treatment with ISO. A significant decrease in EF was observed in WT mice treated with isoproterenol compared to WT. Interestingly, the effect of ISO on EF was abolished in AMPD KO mice. EF was not different between WT and AMPD KO mice not treated with ISO. Moreover, a similar effect was observed with the FS measurement. There was a considerable reduction in FS in the WT group treated with ISO compared to the WT group and a suppression of the ISO impact on FS in the AMPD KO group. FS measurement did not differ between the non-treated WT and AMPD KO groups. Furthermore, a significant increase in left ventricular mass was observed in ISO-treated WT mice compared to WT. In turn, ISO did not affect left ventricular mass in AMPD KO mice. LV Mass did not differ between the untreated animals, WT and AMPD KO. This study shows that reduced AMPD activity has a beneficial effect on cardiac function in isoproterenol-induced heart failure. Possibly the enhanced activation of protective AMPK cascade is likely to be the mechanism. The use of specific AMPD inhibitors may offer significant therapeutic potential.

*Acknowledgements*: Preludium 2018/29/N/NZ4/02259, HARMONIA 2016/22/M/NZ4/00678.

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S6.P18

# THE INFLUENCE OF CANNABIDIOL ON ISOLATED RAT ATRIA UNDER NORMOXIC, HYPOXIC AND REOXYGENATION CONDITIONS

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The antioxidant, anti-inflammatory and antiapoptotic properties as well as the comprehensive mechanism of action of cannabidiol (CBD) may play potential cardioprotective role in myocardial injury. The aim of this study was to examine the effect of CBD on the rate and force of contractions of isolated rat atria under control (normoxia) and hypoxic/reoxygenation (H/R) conditions. The experiments were conducted with atria under basal conditions and in the presence of β-adrenoceptors stimulation with a non-selective agonist isoprenaline (ISO). Both, positive chronotropic (spontaneously beating right atria) and inotropic (electrically stimulated left atria) effects were evaluated. Hypoxia was achieved by replacement of carbogen gas by 95% $N_2$ and 5% $CO_2$ in the organ baths. After 30-min incubation with 1 μM CBD (or its vehicle) atria were exposed to 30 min hypoxia followed by 30 min reoxygenation. The increasing concentrations of ISO (0.01 nM–10 μM) were administered before or after H/R. Atrial rate and force of contractions decreased during hypoxia. Rate of contractions of right atria returned after reoxygenation to values comparable to the basal while the force of contractions of left atria reached approximately 50% of the basal. CBD prevented the decrease in rate of contractions of right atria during the hypoxia (about 50%). However, this protective effect of CBD was abolished by previous adrenergic stimulation with ISO. On the contrary, in left atria stimulated with ISO, CBD accelerated the recovery of left atrial contractile force during reoxygenation in comparison to the tissue not treated with CBD. Additionally, incubation with CBD potentiated the inotropic effect of ISO in left atria given after H/R. In summary, CBD exerts cardioprotective effect and can affect the ability to endure cardiac hypoxia and reoxygenation but in different manner in right and left rat atria.

*Acknowledgements*: The work has been supported by the National Science Centre (Poland), research grant 2019/03/X/NZ7/00446.

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S6.P19

# NEUROPEPTIDE FF COUNTERACTS OPIOID INDUCED RESPIRATORY DEPRESSION

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The activity of opioids undergoes the regulation by a homeostatic anti-opioid system involving i.a. neuropeptide FF (NPFF) - a member of RF-amidated neuropeptides. The contribution of this peptide to the modulation of pain perception, opioid-induced tolerance, and dependence seems to be well documented while there is scarce information about its effect on respiratory pattern and opioid-induced respiratory depression. The aim of the present study was to examine the influence of intracerebroventricular (icv) administration of NPFF on respiration and its effect on post-opioid cessation of breathing (apnea). Urethane-chloralose anaesthetized male Wistar rats spontaneously breathing room air were injected icv with various doses of NPFF 5 min prior to intravenous (iv) endomorfin-1 (EM-1) administration. Respiratory parameters, arterial blood pressure and heart rate were measured. Neither vehicle (saline) nor doses of NPFF (1, 10 and 20 μg) injected into the right cerebral ventricle affected all measured variables. However, icv pre-treatment with NPFF at a dose of 20 μg abolished the presence of post-EM-1 apnea of median duration of 7 s and diminished the maximal drop in the median arterial blood pressure from 30 mmHg to 10 mmHg. These effects were completely blocked by NPFF receptor antagonist - RF9 (20 μg) - given icv in a mixture with NPFF (20 μg) before systemic challenge with EM-1. Our experiments showed that centrally administered neuropeptide FF weakens the respiratory depression induced by icv EM-1 injection. This suggests the important role of NPFF and its receptors localized centrally in the manifestation of vagally mediated opioid-induced apnea.

Acknowledgements: This study was financed by the Polish National Science Center MINIATURA 1 Program (2017/01/X/NZ4/00465).

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S6.P20

# INFLUENCE OF CANNABINOID $CB_1$ AND $CB_2$ RECEPTOR ANTAGONISTS ON CARDIOSTIMULATORY EFFECTS OF ISOPRENALINE IN HUMAN ATRIAL TRABECULAE

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We have demonstrated that cannabinoid $CB_1$ and $CB_2$ receptor antagonists AM251 and AM630 differentially modulate positive chronotropic and inotropic effect of the non-selective β-adrenoceptor agonist isoprenaline in right and left atria isolated from Wistar rats (Weresa *Pharmacol Rep* 2019, 71, 82-89). The aim of the current study was to examine whether the modulatory effects of $CB_1$ and $CB_2$ cannabinoid receptor antagonists on cardiostimulatory effects of isoprenaline will also occur in human atrium. Experiments were carried out in paced human atrial trabeculae (1 Hz) obtained from patients who underwent cardiosurgery. The trabeculae were incubated for 30 min with AM251 or AM630 ( 0.1, 1 or 3 μM). Then concentration response curves for isoprenaline (0.1 nM–30 μM) were constructed. Isoprenaline exerted the concentration-dependent increase in cardiac tissue force (positive inotropic effect). AM251 (0.1 and 3 μM) and AM630 (0.1 μM) decreased the inotropic effects of isoprenaline by about 70%. In contrast, the blockade of $CB_1$ or $CB_2$ receptor with both CB-R antagonists in the intermediate concentration (1 μM) led to increase in force of contraction (by about of 20% for AM251 and 45% for AM630). In conclusion, in human atrial trabeculae, cannabinoid $CB_1$ and $CB_2$ receptor antagonists modulate cardiostimulatory effects of isoprenaline in a different manner, dependent on antagonist concentration. Therefore, due to increasing interests of cannabinoid antagonists as a therapeutic agents we underline that caution should be taken by their application, especially under conditions associated with enhanced sympathetic tone.

*Acknowledgements*: The work was supported by the Medical University of Bialystok, Bialystok, Poland; grant No. SUB/2/DN/19/002/2213.

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